Rev Environ Contam Toxicol 171:111–137

Environmental Impact of Avermectins

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I. Introduction

Terrestrial ecosystems contain a variety of communities comprising populations of diverse organisms, many of which can be important in organic matter breakdown, or in recycling nutrients, or can be pests of crops and animals or predators and parasites of pests. Pesticides can affect both the structure and function of managed and natural ecosystems. They usually tend to decrease ecological diversity and change the relative abundance of particular organisms because of the decreased populations of some groups of organisms and greatly increased numbers of others, which may result from their release from pressure by predators and antagonists.

The avermectins are a relatively new group of insecticidal, acaricidal, and nematicidal pesticides that have been used in agriculture and horticulture to control parasites of domestic animals and pests of cotton, citrus, pears, vegeta-

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Communicated by George W. Ware.

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bles, and ornamentals (Dybas 1989). They are effective against a wide range of mites (Acarina) and insects (Insecta) from such orders as Dictyoptera, Anoplura, Homoptera, Thysanoptera, Coleoptera, Siphonaptera, Diptera, Lepidoptera, and Hymenoptera (Strong and Brown 1987). Avermectins are also commonly used as antiparasitic agents in veterinary medicine and as prophylactics against river blindness (onchocerciasis) in humans (Lindley 1987). However, the most extensive use of these chemicals has been in the control of pests of livestock. They are used regularly as an antiparasitic agent for cattle, horses, swine, and dogs with activity against organisms in the phyla Nemathelminthes and Arthropoda (Campbell et al. 1983; Forbes 1993). For example, horses can be treated as often as 6–12 times per year (Herd et al. 1993). Because innovations in anthelimintic and endectocidal measures have been rare during the past 38 years, avermectins are used extensively to treat a wide variety of parasitic infections in livestock (Williams 1997).

The efficiency and broad spectrum of activity of avermectins make them extremely attractive to farmers, but there have been increasing concerns about the effect of these pesticides on the environment, particularly in terms of soil pollution and organic matter breakdown. For pesticides such as avermectins to have a significant environmental impact, they would have to be toxic to certain terrestrial animals or humans that are exposed to these chemicals, or they could contaminate aquatic or soil environments and have adverse effects on them. Although avermectins can kill aquatic invertebrates or fish, they are very unlikely to reach aquatic systems in significant quantities, and little is known of their impact on wild vertebrates. The primary impact of avermectins on the environment seems usually to result from the use of the pesticide on farm animals, which can result in its excretion in the feces. Livestock feces, particularly those of cattle, provide a microhabitat and breeding ground for a very large number of invertebrate species, the majority of which are insects. The overall impact of avermectins on the structure and function of agroecosystems and their potential for adverse environmental effects is reviewed here.

II. Chemistry and Fate of Avermectins

A. Chemistry and Mode of Action

Avermectins are high molecular weight, hydrophobic compounds that are active against a variety of animal parasites and insects. They are macrocyclic lactones isolated from a fermentation broth of the soil actinomycete *Streptomyces avermitilis*. The avermectin complex consists of four major components (A_{1a}, A_{2a}, B_{1a}, and B_{2a}) and four minor homologous components (A_{1b}, A_{2b}, B_{1b}, and B_{2b}). Mixtures of the homologous substances containing 80% or more of the 'a' and 20% or less of the 'b' are referred to as avermectins A_1, B_1, A_2, and B_2 (Campbell 1985). Avermectin B_1, commonly known as abamectin, is a potent broad-spectrum chemical and has been used against a variety of insect pests in horticulture. Ivermectin (22,23-dihydroavermectin B_1) is a synthetic derivative of the

naturally occurring avermectin B_1 (80% B_{1a} and 20% B_{1b}) that is used mostly to control livestock parasites.

Avermectins (abamectin and ivermectin) are broad-spectrum pesticides, reported to be toxic to 84 pest species (Campbell 1985; Strong and Brown 1987). Avermectins amplify the effect of the ligand glutamate on the chloride ion channels of invertebrates. At high concentrations, avermectins can cause irreversible opening of these channels (Rohrer and Arena 1995). These chemicals act on inhibitory neuromuscular synapses, stimulating the release of transmitter gamma-aminobutyric acid (GABA) and enhancing the binding of GABA to muscle membranes, resulting in hyperpolarization of the muscle (Campbell 1985), thus producing paralysis and eventual death. Contraction of the pharyngeal muscle is a symptom of this hyperpolarization (Brownlee et al. 1997).

B. Environmental Breakdown And Fate

Alvinerie et al. (1999), Campbell et al. (1983), and Herd et al. (1996) reported that in both sheep and cattle only a portion of the ivermectin dose that is applied is metabolized, most of it being excreted unaltered in their feces. This portion may be up to 70% in sheep, according to Steel (1993). There are as many as 13 metabolites, the main ones being probably monosaccharid- and aglyconderivates of the 24-hydroxy-methyl-metabolite of ivermectin (Halley et al. 1989b). For aquatic organisms such as *Daphnia*, the metabolites of ivermectin seem to be less toxic than the parent compound (Bloom and Matheson 1993), but we do not know if this is the case for terrestrial organisms.

Some physicochemical key properties of ivermectin and abamectin are summarized in Table 1. According to these parameters, avermectins are virtually nonvolatile and have a very low water solubility with a strong affinity to attach to lipids, soil, and organic matter. No residues have been found in water passing through soil leaching columns. Therefore, when the dung containing ivermectin is mixed into soil beneath or adjacent to pats the ivermectin tends to bind tightly to the organic matter in the feces and can persist in soils or organic media for several months, or even possibly years, particularly under anaerobic conditions

Table 1. Physicochemical properties of avermectins according to various authors (Halley et al. 1989b, 1993; Bloom and Matheson 1993; Sams 1993).

Parameter	Ivermectin	Abamectin
Log P_{OW}	3.22	3.99
BCF_{Fish}	54 (estimated)	74 (measured)
K_{OC} (estimated)	12,660–15,700	5,300–6,600
Water solubility	1–4 mg/L	?
Volatility	$<1.5 * 10^{-9}$ mmHg	?
Photolysis in water	<0. 5 d	<0. 5 d

(Halley et al. 1989b, 1993). There are considerable variations in the available data related to persistence of avermectins in soil or dung due to various experimental variables. Halley et al. (1989a) reported that the environmental 'half-life' of ivermectin in a soil-feces mixture was 90–240 d in the laboratory. Under field conditions in summer, the surface residue would be degraded rapidly, by photodegradation and microbial activity under the influence of sunlight and soil microbes, with a degradation half-life of 2–8 wk in soils (Halley et al. 1989b). However, in winter Lumaret et al. (1993) reported that ivermectin degraded more slowly outdoors, with 'half-lives' from 91 to 217 d (or even up to 365 d; Bloom and Matheson 1993). For abamectin, 'half-life' values between 14 and 56 d have been reported (Halley et al. 1993). Therefore, the excreted ivermectin, which is insecticidal in nature, can remain active in cow dung on average for approximately 2 mon after exposure on pasture (Madsen et al. 1990) but has the potential to persist much longer, even into the following season, particularly in colder climates. The high lipid affinity of avermectins raises the possibility that they might bioaccumulate in food chains, but this has not been demonstrated in studies currently available.

The results of degradation studies of ivermectin residues in dung so far are difficult to compare in detail because the experimental test conditions differed greatly in terms of temperature, soil type, and source of dung. Hence the need for a standardized method of assessing degradation rates became obvious (Bouwman and Reus 1994). However, until now only an improved method for estimating the fate of veterinary drugs in dung and soil is available (Spaepen et al. 1995).

C. Ivermectin Concentrations in Soil and Dung

To assess the potential environmental risks of compounds such as ivermectin it is necessary to define their probable concentrations in the environment. However, this depends on both the method of application and the dose applied. Obviously the best way is to measure residues directly under realistic field conditions. For example, depending on the method of application of ivermectin, Sommer et al. (1992) reported residues of ivermectin in dung of 0.4–9 mg/kg and stated that there was no apparent degradation of ivermectin in dung after 45 d of exposure in the field. Two days after the application of 0.3 mg of ivermectin/kg body weight of cattle, the concentrations of ivermectin in cow dung (including metabolites) were approximately 800 μg/kg and after 7 d 270 μg/kg (Chiu et al. 1990; cited in Steel 1993). After an injection of 0.2 mg/kg body weight to heifers, Sommer and Steffansen (1993) detected, during a period of 5 d after application, about 3 mg/kg in the dung, but after 14 d only 0.3 mg/kg remained. After external applications of 0.5 mg/kg body weight to cattle, higher initial concentrations were found in the dung. These concentrations, however, decreased so rapidly that, after 14 d, no ivermectin was detectable. According to Sams (1993), a similar reduction occurred after oral applications of 0.2 mg/kg body weight to horses: 1 d after application the concentration was ap-

proximately 5 mg/kg fresh weight, but just 2–3 d later less than 0.05 mg/kg could be measured.

If adequate field measured values are not available, the environmental concentrations of ivermectin have to be estimated [=Predicted Environmental Concentration (PEC)]. For housed animals a standardized procedure has been proposed in the European Union (Spaepen et al. 1995), which is based on parameters such as the amounts of the pesticide applied, numbers of applications per year, the numbers of treated animals, and their average body weight. Afterward the concentrations of the compound in the feces of the animals is calculated. As a last step, the concentrations in the soil of those agricultural areas treated with the dung can be estimated. By using additional factors such as degradation rates it is possible to refine this "worst case" situation. A comparable procedure has also been used in the U.S. (Mangels 1995).

Based on such methods, the concentrations of ivermectin in soil that result from incorporation of treated dung following external applications to various livestock species should range from 0.09 to 0.51 µg/kg and after injections between 0.27 and 5.1 µg/kg (Bloom and Matheson 1993). According to Halley et al. (1989b), reported values are even lower: 0.001–0.09 µg/kg, e.g., taking the storage time of dung into consideration. However, if the dung should be used very quickly (e.g., after only 7 days of storage), ivermectin concentrations of 0.035–0.35 mg/kg could be reached in pig dung (Halley et al. 1989b). Our estimates, based on the formula provided by Spaepen et al. (1995), led to "worst case" concentrations between 0.1 and 10 µg/kg soil, depending on the treated animal, the number of applications, and so on (Römbke et al. 1996). Nevertheless, it should be kept in mind that, in a wide range of reported data, the initial concentration of ivermectin in dung was of the order of magnitude of several mg/kg and in soil of several µg/kg and that the residues are relatively persistent in both soil and dung.

In aquatic systems, ivermectin binds tightly to sediment or particulates. Davies et al. (1998) reported that the 'half-life' of ivermectin in marine sediments was more than 100 d. When ivermectin occurred near the surface of open water bodies, it was quickly subjected to photodegradation and biotransformation to less active compounds (Bloom and Matheson 1993; Halley et al. 1993).

With respect to abamectin, Wislocki et al. (1989) reported its rapid degradation in the environment and a lack of accumulation and persistence in both terrestrial and aquatic environment.

III. Environmental Effects

A. Crop Pests and Beneficial Insects

The sublethal effects of abamectin on crop-inhabiting insects include: behavioral modifications such as increased activity, feeding inhibition, torpor, reduced fecundity, morphological aberrations, and decreased fertility and sterility effects (Strong and Brown 1987). Abamectin provided excellent control against the

two-spotted spider mite, *Tetranychus urtica* Koch (Putter et al. 1981) and the striped cucumber beetle, *Acalymma vitatum* (F.) (Reed and Reed 1986). Cox et al. (1995b) and Grafius and Hayden (1988) found that abamectin effectively controlled *Liriomyza trifolii* larvae and prevented their emergence as adults. The pesticide caused high mortality of all larval stages and no adults emerged successfully. Glancey et al. (1982) found that abamectin can irreversibly sterilize the fire ant *Solenopsis invicta* Buren by causing cell and tissue damage to the queen's ovaries. Abamectin also exerts an inhibitory effect on the oviposition and hatch of *Drosophila melanogaster* and *Lobesia botrana*. It can affect the larvae and the adults of both species, the larvae being more susceptible than the adults (Ishaaya et al. 1986). Abamectin reduced the fertility of both *Ceratitis capitata* and *Dacus cucurbitae* after topical treatment of the insects (Albrecht and Sherman 1987). When injected into the pseudostem of banana, abamectins effectively reduced nematode infections (Jansson and Rabatin 1997) of the plant.

Deecher et al. (1987) suggested that abamectin is efficacious as a control agent for the management of the gypsy moth. The chemical applied at 100 ppm reduced the hatch of the gypsy moth eggs markedly and caused 100% mortality of the larvae. It was also effective at reducing populations of diamondback moth (*Plutella xylostella*) that were resistant to other pesticides (Lasota et al. 1996). However, repeated exposure to abamectin induced resistance in the diamondback moth (Wright et al. 1995). A single application of abamectin was enough to prevent the entry of codling moth (*Cydia pomonella*) larvae into apples, but the control did not reach a commercially viable level compared to azinphosmethyl (Cox et al. 1995a). Campos et al. (1995, 1996) demonstrated that *Tetranycus urticae* Koch developed a 13- to 1597-fold resistance to abamectin after 38 selection cycles in the laboratory, but no resistance changes could be observed in the field. On the other hand, Shipp et al. (2000) found that abamectin was only slightly toxic or nontoxic to commercially produced mites used for pest control in greenhouse trials. Park et al. (1995) demonstrated that abamectin was much less toxic to predatory mites than to spider mites. Grafton-Cardwell and Hoy (1983) reported that abermectin did not affect the fertility of the western predatory mite. When applied at the recommended field rate, abamectin showed little toxicity to beneficial arthropods, affecting pests of citrus with mortality never exceeding 10% (Morse et al. 1987).

Abamectin is likely to affect many nontarget insects and even possibly to induce resistance in insect pests in much the same manner as many other synthetic pesticides. Tzeng and Kao (1999) reported that spraying with abamectins caused 80%–99% mortality in *Eretmocerus orientalis* adults, a parasitoid of the silverleaf whitefly, *Bemisia argentifolii*. El-Bagoury and El-Banhawy (1987) studied the effect of feeding abamectin-poisoned prey against a predaceous mite *Phytoseius fenitimus* Ribaga, an important natural enemy on deciduous fruit trees in Egypt. They reported that mortality of the predator increased progressively by lengthening its time of feeding. Reproduction in mites exposed to abamectin continued at lower rates compared with those in the control.

B. Livestock Pests

Although originally developed to eradicate gastrointestinal and pulmonary nematodes in domestic animals, ivermectin is effective in killing many ectoparasitic insects, as well as endoparasites such as larvae of *Gasterophilus* (Campbell 1985). Ivermectin is active systematically against a variety of livestock pests, including lone star ticks, grubs, mites, and lice feeding on cattle (Drummond 1985). Miller et al. (1989) observed that a daily dose of ivermectin of 20 μg/kg administered to Spanish goats was sufficient to result in a reduction of more than 95% of estimated larvae of lone star ticks. James et al. (1980) reported that wool saturated with ivermectins protected sheep from the first-stage larvae of *Lucilla cuprina.* Pigs and sheep infected with mange had a 100% reduction in infection after treatment with ivermectin (O'Brien et al. 1999; Pereira and Kohek 1998). Daily oral doses of 35 and 50 μg/kg/day of ivermectin to white-tailed deer resulted in 100% control of adult ticks and 90% control of nymphs that were placed on treated fawns (Miller et al. 1989). Intraruminal controlled-release boluses of ivermectin administered to sheep provided 100% protection against sheep scab, *Psoroptes ovis* (Forbes et al. 1999), nasal bots, *Oestrus ovis* (Rugg et al. 1997), fecal strongyle, *Nematodirus*, and *Trichuris* (Rehbein et al. 1999). A similar bolus administered to cattle significantly reduced their gastrointestinal nematode counts (Johal and Kaur 1995; Munyua et al. 1998; Pitt et al. 1996). Miller and Morrison (1992) reported that ivermectin was effective in decreasing infestations of strongylate nematodes in calf feces. Paulrud et al. (1997) reported that a 99% reduction in strongyle worm egg output was recorded in the feces of horses treated with ivermectin. Similar effects of ivermectin were reported in pigs infected with strongyles (Barth et al. 1996). Ivermectins were 100% effective against *Oestrus ovis* infestations in sheep (Lucientes et al. 1998). A pour-on formulation of ivermectin of 500 μg/kg administered to cattle proved 100% effective against gastrointestinal nematodiasis (Islam et al. 1999). Adult *Stomxys calcitrans* and *Haematobia irritans* were not very responsive to systemic ivermectin circulating in the blood of their hosts, while *Glossinia palpalis* died within 4–8 d of feeding daily on goats or guinea pigs dosed with ivermectin (Distelmans et al. 1983). However, according to Guglielmone et al. (1999), the *Haematobia irritans* infestations of cattle injected with 200 μg/kg ivermectin were reduced by 51% to more than 73%. A topical administration of ivermectin at a dose of 500 μg/kg was reported to be 100% effective against *H. irritans* infestation by Uzuka et al. (1999). Certain gastrointestinal nematodes, such as *Trichostrongylus colubriformis* and *Ostertagia circumcincta,* demonstrated resistance to ivermectin; their LD_{50} increased steadily during a 35-d test trial (Gopal et al. 1999).

C. Dung Fauna

Animal dung is broken down by a range of specialized invertebrates including insects, other arthropods, and earthworms. Significant amounts of ivermectin and its residues are eliminated in livestock feces. Once deposited, the chemical

does not decompose rapidly. The chemical binds tightly to organic matter within the pat, and retains its biological activity from a few weeks to more than a year, once deposited on grazing land. For instance, Halley et al. (1989a) stated that the environmental half-life of ivermectin in a soil–feces mixture was 90–240 d in the laboratory and that decomposition was delayed in the winter. Moreover, the presence of ivermectin in the dung can be detrimental to many species of dung insects, regardless of whether they are pests or beneficial species that break down the organic matter. Under drought conditions, Krueger and Scholtz (1998) reported that ivermectin decreased species diversity and increased certain species dominance in dung. These conditions persisted for 3 mon after the termination of ivermectin treatment to the cattle. Halley et al. (1993) stated that in general the toxicity of ivermectin and avermectin residues in dung is species dependent and that the larvae of beetles and flies are more sensitive to residues than adults.

The overall impact of avermectins on insects that live in dung was reviewed by Strong (1993). He concluded that, following the treatment of animals, ivermectin is eliminated in livestock feces where it also has a wide range of harmful effects on characteristic insects that breed in dung, most of which fauna are beneficial. The effects range from acute toxicity in larvae and adults through disruption of metamorphosis to interference with reproduction. Different methods of ivermectin administration can lead to different concentrations of residues in the feces, which in turn influences the responses of nontarget organisms. Higher Diptera seem to be particularly sensitive to drug residues, demonstrating a wide range of responses from the death of larvae to developmental abnormalities in the adults. Some larvae and immature adult beetle species die in the dung of recently treated animals, and delayed effects upon reproduction and physiology have been observed in adults feeding on dung after longer posttreatment times. Although the impact of lethal doses has been described for some species, the effects of sublethal doses have hardly been recognized at the present time.

Correlated with deleterious effects of ivermectin on dung-breeding insects, a retardation in the rate of loss of biomass of dung pats from ivermectin-treated cattle has been observed following the various forms of administration. Strong (1993) concluded that differences in methodology, inappropriate statistics, or extremes of climatic conditions prevailing at the time of testing could explain the results of those studies in which such delays have not been observed.

Ivermectin has been shown to have considerable insecticidal activity against dipteran larvae and beneficial insects that invade the feces (Wall and Strong 1987, 1988). Orally administered ivermectin is usually eliminated from the dung more rapidly than injected ivermectin and is likely to be less harmful to the dung fauna (Wardhaugh and Mahon 1998). However, the same authors reported that for abamectin or ivermectin bioassays survival of the bush fly (*Musca vetustissima*) was depressed for 32 d. Wall and Strong (1987) observed that dung from cattle treated with ivermectin remained almost arthropod sterile for more than 3 mon when exposed on pasture. Lumaret et al. (1993) and Barth et al. (1994) found significant reductions in numbers of Diptera larvae in soil samples

under treated dung when ivermectin was detectable in the dung. Strong (1989) and Strong et al. (1996) reported that ivermectin could disrupt the development of higher Diptera, many of which are important inhabitants and decomposers of cattle dung and which are exposed to ivermectin and its residues when cattle have been treated with the pesticide. The author found that the development of the fly *Calliphora vomitoria* was affected by ivermectin in four different ways: interference with pupation, suppression of adult head development, inhibition of emergence from the puparium, and disruption of ovarian development in the adult female. The chemical was reported to prevent the breeding of dung-dwelling flies such as horn flies (*Haematobia irritans*), stable flies (*Stomoxys calcitrans*), houseflies (*Musca domestica*), face flies (*Musca autumnalis*) (Fincher 1996; Miller et al. 1981; Wardhaugh et al. 1996), and dung flies (*Neomyia cornicina*) (Gover and Strong 1995, 1996), all of which are flies attacking cattle.

When horn flies were reared on dung from cattle treated with 200 mg/kg, adult emergence was decreased by 78.7%–100% for 8 wk. In laboratory tests, these effects occurred at environmentally relevant concentrations (e.g., 0.2 mg/kg; Schmidt 1983). Fincher (1996) reported delays in emergence of dung beetles from feces of steers treated with ivermectin for up to 3 wk and horn flies for 5–6 wk. Krueger and Scholtz (1995) observed that dung from cattle that were treated subcutaneously with ivermectin prevented the development of *Musca nevilli* in it for 4 wk and reduced the fertility of flies emerging successfully after 4 wk. Krueger and Scholtz (1997) reported that 200 mg/kg of ivermectin prolonged the development of dung-breeding beetles for up to 28 wk. Madsen et al. (1990) reported that even 90 d after treatment adverse effects in dung on the fly *Musca vetustissima* occurred. Clarke (1992) reported morphological changes (using fluctuating asymmetry) in adults when the larvae developed in cattle dung from animals treated with 0.2 mg/kg body weight of avermectin B_1, even 11 wk after application of the compound. The results of this test using a morphological parameter were clearly more sensitive than those obtained from mortality tests performed with the same species and under the same test conditions. In mortality tests, 8 wk after application fly populations reached control level (Ridsdill-Smith 1988). Such toxic effects were not observed in midge larvae (Nematocera) tested at the same time. This difference is probably caused by the different behaviors of these insects and, therefore, exposure situation of the two insect groups: Nematocera flies use the dung at a later stage than other fly larvae and so are exposed to lower concentrations of the chemical. McCracken and Foster (1993) found that ivermectin markedly changed the fauna in and below dung-treated pats at concentrations between 0.5 and 2 mg/kg. The chemical particularly affected cyclorrhaphan fly larvae (Sepsidae, Muscidae, and Sphaeroceridae) at concentrations of approximately 0.5–4 mg/kg (Schaper and Liebisch 1991). Bioassays with houseflies of dung from cattle, treated with ivermectin, resulted in suppression of fly emergence for 11 d post treatment (Marley et al. 1993).

Miller et al. (1989) observed that horn fly emergence was reduced 50% when the manure from goats that had been treated orally with ivermectin was mixed

with untreated cow manure. In Denmark, the development of horn flies and face flies was inhibited for 13–14 d following pour-on treatment of cattle with ivermectin at doses of 0.5 mg/kg body weight (Sommer et al. 1992). Gover and Strong (1995) reported that ivermectin in dung reduced the ovipositia of dung flies (*Neomyia cornicina*) as well as the percentage hatch. Schmidt (1983) reported a 96% reduction in the emergence of sphaerocerid flies and parasitic Hymenoptera from treated cattle dung. Similarly, Strong (1993) observed that ivermectin residues in the dung affected the density of several species of Diptera and Coleoptera colonizing the cattle dung. The larvae in both orders were more susceptible to the drug than adults, e.g., in the dung beetle, *Aphodius* sp. (Strong 1992; Strong and Wall 1994). McCracken (1993) expressed particular concern regarding the impact of ivermectin on rare insect species associated with the dung-like *Stercoricolous* beetles (i.e., species of *Copris* and *Onthophagous*). Ivermectin affected the survival of the bushfly, *Musca vetustissima* Walker, a nuisance pest of man and animals, and the breeding of the dung beetle *Onthophagus binodis* Thunberg, a beneficial insect introduced to Australia to increase the rate of breakdown of cattle dung and dispersal on pastures (Ridsdill-Smith 1988). Numbers of other dung beetles of the genus *Aphodius* (Scarabaeidae) were affected in fresh dung (i.e., 1–2 d after treatment) but not 14 d after treatment (Strong and Wall 1988). Dadour et al. (1999) and Krueger and Scholtz (1997) found that postinjection ivermectin residues in dung significantly decreased dung dispersal activity by adult dung beetles. On the other hand, Fincher (1992) found that ivermectin, applied to cattle at the recommended rate of 200 μg/kg, did not cause any mortality in adult dung-burying or predaceous beetles reared on dung from treated animals. Sommer et al. (1993b) reported clear differences in sensitivity between two closely related species of African dung beetles (Scarabaeidae): After a subcutaneous injection of 0.2 mg/kg body weight of ivermectin to heifers, larvae of *Onthophagous gazella* died in dung up to 8 d after treatment, whereas larvae of *Diastellopalpus quinquedens* developed successfully in the same dung.

Ivermectin in dung may also interfere with insects that parasitize, prey on, or compete with the immature stages of flies that develop in cattle dung (Fincher 1992). Pupae of the common housefly *Musca domestica* Linnaeus exposed to 0.25 ppm of ivermectin were parasitized less by *Muscidifurax zaraptor* Kogan (Floate and Fox 1999). However, when the dosage was decreased to 0.01 ppm, parasitism increased above the control levels. Barth et al. (1993) reported that the numbers of dung-specific nematodes in dung pats derived from cattle treated with ivermectin were reduced. However, earthworm density present in dung was not affected by avermectin (Strong 1993).

D. Soil-Inhabiting Invertebrates

Avermectins are never applied to soil to control pests other than fire ants, but can be expected to reach soil through fallout from foliar spraying for plant pests. They could also reach the soil from incorporation of animal dung deposited on

the soil surface. Soil-inhabiting invertebrates are most important in breaking down organic matter, incorporating it into soil, and releasing the mineral nutrients that it contains. There have been no direct investigations into the effects of avermectins on populations of soil-inhabiting invertebrates, although there are extensive data on their effects on some aboveground invertebrate taxa, especially insects, that can be used to predict possible effects on soil-inhabiting invertebrates.

There is no evidence in the literature on the effects of avermectins on soil-inhabiting mites (Acarina), but because avermectins are toxic to many closely related arachnids they may well have adverse effects on some species of soil-inhabiting mites. There is a need for further investigations into these effects because these invertebrates are important in organic matter breakdown in soil. With respect to insects, a wide range of beetles (Coleoptera) are killed by avermectins, particularly abamectin, but few data are available on the effect of avermectins on soil-inhabiting Coleoptera although there is an abundance of literature demonstrating adverse effects on dung beetles. There is a very extensive literature on the effects of avermectins on fly larvae (Diptera). Ivermectin is particularly toxic to almost all groups of Diptera, particularly larvae. There are considerable data on the toxicity of avermectins to the imported red fire ant, which is a true soil-inhabiting species. Even low doses of abamectin (0.0055%) caused the ants to abandon their colonies and resulted in severely impaired reproductive performance (Apperson et al. 1984). As avermectins are toxic to an extremely broad range of insects, it can be expected that they kill many nontarget soil-inhabiting insects (Strong and Brown 1987). On the other hand, Barth and Schaper (1992) reported that soil-inhabiting nematodes—in contrast to parasitic species—were not affected by ivermectin.

Avermectins do not appear to be extremely toxic to earthworms in soil and dung. The 28-d LC_{50} toxicity of ivermectin was 315 mg/kg in soil and the NOEL was 12 mg/kg; the 28-d LC_{50} of avermectin was 28 mg/kg (Wislocki et al. 1989). However, earthworms treated with invermectin at a range of doses lost weight compared with the control earthworms, and earthworms exposed to 200 mg/kg lost weight over the entire 28-d exposure period. Gunn and Sadd (1994) investigated the effect of ivermectin on the earthworm *Eisenia fetida*, which is a species that breaks down organic matter such as animal dung. They tested concentrations of 2, 4, 8, 12, 16, 20, and 60 mg/kg in soil compared with an uncontaminated control using the OECD test protocol (1984). They reported that concentrations similar to those found in the feces of treated animals caused mortality and decreased growth rates of the earthworms. Concentrations greater than 20 mg/kg had a marked deterrent effect, inhibiting the earthworms from entering contaminated soil. Gunn and Sadd considered the most serious effect to be reductions in cocoon production: earthworms exposed to 4 mg/kg produced 50% fewer cocoons over 21 d. Madsen et al. (1990) investigated the effects of ivermectin in dung from heifers treated with 200 mg/kg of the pesticide on eight species of lumbricid earthworms. Although there was some depres-

sion of the different species from 1 to 20 d after treatment, the results were not statistically significant.

E. Dung and Organic Matter Breakdown

The breakdown of organic matter in soil and the recycling of nutrients that it contains are key processes in maintaining soil fertility. Knowledge of the effects of pesticides on these dynamic processes is important if we are to avoid loss of fertility in grazed pastures.

Halley et al. (1989a,b, 1993) considered that although there is such a strong body of evidence that ivermectin has adverse effects on insects that inhabit dung, they did not consider degradation of dung pats in field conditions, and concluded that overall effects on dung-associated insects are limited. However, Strong (1993) disagreed strongly with this conclusion as well as the claim by Halley et al. (1989a) that any reductions in numbers of dung-inhabiting insects of the dung pats are temporary, although such recolonization has never been demonstrated. Various workers have identified between 67 and 123 nonpest insect species in cattle dung pads, most of which are beneficial insects, important in breaking down and recycling dung resources (Anderson et al. 1984). Fly larvae and beetles, together with a diverse microfauna, are the primary decomposers of cattle dung pads. In addition, a wide range of invertebrates are involved in degradation of animal dung, including earthworms (Oligochaeta), springtails (Collembola), mites (Acarina), and nematodes (Nematoda). It should be noted that the importance of each of these groups can vary considerably depending on various abiotic factors such as climate, moisture, and exposure (Barth 1993). The tunneling and feeding activities by insect larvae and other invertebrates in dung pads are critical in promoting desiccation, aeration, and microbial activities (fungi and bacteria), which eventually leads to complete degradation and disappearance of the dung pads. Anything that kills these organisms or interferes with their activity can have a serious impact on the overall rates of breakdown of dung. Strong (1986) suggested that the fauna responsible for dung degradation and recycling could be damaged as a side effect of ivermectin treatments of livestock. Cattle fecal pats containing ivermectin degraded more slowly than those not containing the compound (Wall and Strong 1987; Madsen et al. 1990).

Ivermectin in dung was reported to kill nontarget organisms and cause undesirable environmental consequences by affecting dung-inhabiting insects involved in degradation of pats on pasture (Wall and Strong 1987). Strong (1992) reported that cow pats decomposed within one grazing season, due to the aerating effects of Diptera followed by the activity of Coleoptera and annelids. However, because insect activity is disrupted ivermectin can be expected to have effects on rates of dung pat degradation. Wall and Strong (1987) reported that dung collected 2 wk after treating calves with ivermectin and exposed in the field for 100 d, contained fewer insects and failed to degrade normally; this could have resulted from direct effects of the chemical on the survival of dung-

feeding invertebrates or decreased rates of insect colonization. Madsen et al. (1988) reported a pronounced delay in the disappearance rates of cattle dung treated with ivermectin, attributed to the negative effect of the chemical on dung-living dipterous larvae. These authors concluded that a single ivermectin treatment was sufficient to eliminate dung-dwelling Diptera for at least 30 d.

Holter et al. (1993) and Floate (1998) reported that ivermectin therapy of livestock can affect the rates of dung colonization and thus decomposition by attracting or repelling dung beetles. Sommer and Nielsen (1992) observed that dung containing ivermectin concentrations of at least 1.6 ppm (dry wt) was lethal to larvae of the dung beetle *Onthophagus gazella* F., which is essential for cow dung degradation. This change would result in a decrease in the rate of dung burial by these beetles, which in turn would negatively affect the sustained fertility of pastures. On the other hand, Wardhaugh and Mahon (1991) found that dung from animals treated with avermectin attracted more beetles than dung from untreated animals, and that departure rates of beetles from treated dung were lower than those from untreated dung. This effect may be potentially harmful; if the beetles have no obvious ability to discriminate by smell or taste, they may be even more vulnerable to avermectin residues. However, burial activity was more rapid in the treated dung pats, resulting in a greater rate of dung degradation compared to dung from nontreated cattle. Sommer et al. (1993a) reported that the amounts of cattle dung buried in the field by the dung beetle *Diastellopalpus quiquedens* Bates were not affected by cattle treatment with ivermectins. However, the numbers of beetle larvae developing in the dung were reduced.

Insect larvae do not contribute to dung decomposition by direct decomposition of organic matter. However, insects mix and aerate the dung pat, which may attract earthworms and enhance breakdown further (Holter 1983). Wall and Strong (1987) reported that earthworms coming to older dung from under the pat were not influenced by ivermectin. Bloom and Matheson (1993) reported that the chemical did not cause any pathological symptoms or behavioral changes in the earthworm *Eisenia fetida* (Savigny) when exposed to several concentrations of ivermectin in soil. Halley et al. (1993) found that avermectins were unlikely to be toxic to earthworms, with LC_{50} values of 315 ppm and 28 ppm in soil, for ivermectin and abamectin, respectively. However, Gunn and Sadd (1994) observed that ivermectin could have a serious effect on pastureland earthworm populations. Concentrations of the chemical, similar to those found in the feces of the treated animals, caused mortality and reduced growth of the earthworm *Eisenia fetida*. High concentrations of the chemical in the dung (20 mg/kg dry wt soil) inhibited earthworms from entering or remaining in contaminated soil. In soil containing 4 mg/kg dry wt soil ivermectins, earthworms produced 56% fewer cocoons than earthworms in ivermectin-free soil. The use of different test substances (pure ivermectin versus a formulated version) and different exposure situations could have been responsible for the different results.

Microorganisms contribute significantly to dung degradation. If avermectins hinder insect activity, the microorganisms cannot easily reach the center of the

dung, and decomposition would be delayed (Strong 1992). However, few pesticides have significant effects on microbial populations. For instance, Burg and Stapley (1989) found that avermectins did not possess any significant antibacterial and antifungal activity except at extremely high concentrations. Soil containing 30 ppb ivermectin in feces from ivermectin-treated steers had no effect on nitrification or soil respiration (Halley et al. 1989a). Similarly, Bloom and Matheson (1993) reported that ivermectin residues in pasture and forest soils appeared to have no significant effect on soil respiration and nitrification. Moreover, abamectin did not affect nitrogen-fixing bacteria even at levels higher than those that would be normally present in the environment (Wislocki et al. 1989). In laboratory tests, only concentrations as high as 11 mg/kg soil caused an increase in microbial respiration and biomass (Pfeifer et al. 1998).

In contrast to the data presented so far, some authors have concluded from their research that avermectins do not affect dung degradation and disintegration appreciation. As McCracken and Foster (1993) mentioned, this might result in part because the effect is less when the climatic conditions favor a quick degradation of ivermectin in the dung. The manure from cattle treated with ivermectin appeared to disintegrate physically at the same rate as that from untreated animals (Schmidt 1983). McKeand (1988) found no difference in the breakdown of feces from cattle receiving three ivermectin treatments compared to feces from untreated cattle. Wratten et al. (1993) and Barth et al. (1993) reported that the insecticidal activity of ivermectin did not retard dung decomposition. These authors concluded that adult dung beetles were much less sensitive to the effects of the ivermectin than their larvae. The earthworms were not affected by the ivermectin in the dung pats. Based on an evaluation by King (1993b), the biannual treatment of sheep with ivermectin seemed to have no detrimental effects on nutrient cycles of an Australian meadow.

These divergent results may be caused by the following factors (Herd 1995):

The different effects of the various ivermectin formulations (oral, injection, slow-release bolus) and ivermectin concentrations

Specific composition of the respective dung fauna (e.g., the proportion of the very sensitive cyclorraphous flies) or differences between biogeographic regions

Climatic conditions—at low activity levels of the dung species (e.g., during dry periods), any effects are difficult to determine

The effects of ivermectin on the decomposition of dung are difficult to review because nearly all investigations have been performed using very different methods. Therefore, it is necessary to standardize the test conditions in future field or laboratory studies. Existing proposals, e.g., for studying litter decomposition, should be used for this purpose.

It seems clear that the overall effects of ivermectin residues on the rates of dung degradation are complex and vary according to the invertebrate species associated with a particular dung degradation process and with the susceptibility of these invertebrates to ivermectin residues. In some cases, the slow rate of

degradation of dung from ivermectin-treated cattle has led to seriously contaminated pastures of low productivity. Herd (1995) estimated that horses and cattle avoid an area six times larger (on average) than the slow-degraded dung pad itself. Anderson et al. (1984) concluded that if ivermectin was used on cattle in California, other than between mid-June through September, the contaminated dung pads they produced would extend degradation by 4–21 mon and require between 3 and 4 yr to degrade. Ewert et al. (1991) found that multiple ivermectin treatments did not have any deleterious effect on the overall pasture ecosystem (i.e., prolonged dung degradation leading to increased pasture fouling) but did result in decreased grazeable pastureland. In spite of the variability in experimental results, sufficient data are available to conclude that invermectin has the potential to retard dung degradation seriously and possibly for long periods under suitable conditions, so this should be considered as a potential adverse environmental effect. If ivermectin becomes widely used on pastured animals, the fouling of grassland by undecomposed dung could have considerable environmental and economic consequences.

F. Plants

Bloom and Matheson (1993) and Halley et al. (1993) found that the avermectins have no phytotoxic effect on plants; the chemical is not translocated significantly into plants from the soil or when sprayed directly on plants. However, avermectins are more readily absorbed into younger plant leaves in growth or sexual states, leading to higher mortality of parasites (Beers et al. 1996; Walsh et al. 1996).

G. Aquatic Organisms

Free ivermectin in water may adversely affect fish and some water-inhabiting organisms such as crustaceans on which they feed. The freshwater aquatic species *Daphnia magna* was the most sensitive species to ivermectin and abamectin. Even more sensitive was the marine crustacean *Mysidopsis bahia*: concentrations that affected this crustacean were in a range of 0.0035–0.0093 μg/L (Campbell 1989). Fish such as rainbow trout and bluegill sunfish were less susceptible to the chemical than was *Daphnia*. Avermectins did not bioconcentrate into fish (Bloom and Matheson 1993; Halley et al. 1993; Van Den Heuvel et al. 1996). Hoy et al. (1992) treated Atlantic salmon orally with radioactive ivermectin against parasitic "sea lice." Due to side effects, such as accumulation of the substance in the central nervous systems of the fish or mortality (starting at 0.4 mg/kg body weight), the compound was not recommended for aquaculture purposes.

Sediment-inhabiting organisms are particularly sensitive to avermectins. Ivermectin used to treat sea lice infestation in salmon had significant effects on a benthic community, including 100% mortality of *Hediste diversicolor* and *Corophium volutator* (Collier and Pinn 1998). Species abundance and biomass variations were also observed. Ivermectin also had high toxicity to the amphipod

Corophium volutator and the starfish *Asterias rubens* (Davies et al. 1998). The sediment-dwelling polychaete *Arenicola marina* had reduced rates of cast production and reduced ability to rebury itself in sediment after exposure to 0.010 mg/kg ivermectin (Thain et al. 1997). These effects are probably indicative of the susceptibility of other sediment-dwelling polychaetes as well. However, ivermectin used to treat infected salmon had few detrimental effects on the mysid shrimp *Neomysis integer* and did not bioaccumulate significantly in the mussel *Mytilus edulis* (Davies et al. 1997).

Abamectin caused a temporary population reduction of invertebrates in a man-made pond. Nauplius and Copepoda populations were decreased by more than 90%, while Rotifera and chironomid species were not affected. Young Coleoptera and Hemiptera were affected adversely whereas adults were not (Ali et al. 1997).

H. Vertebrates, Mammals, and Birds

Avermectins are considered to be relatively safe to mammals. Davis et al. (1999) demonstrated that ivermectin administered to several inbred strains of mice did not affect their general health, body weight, motor coordination, swimming behavior, or spatial learning. However, sensitive behavioral tasks were affected. Some breeds of dogs and some cattle have shown toxic reactions after treatment with recommended doses (Pulliam and Preston 1989). In addition, cattle have gained weight faster and reached sexual maturity at a younger age when treated with ivermectin (Larson et al. 1995; Meija et al. 1999; Whittier et al. 1999). However, reindeer did not have any weight gain after treatment with ivermectin (Oksanen et al. 1998). Sheep drenched with ivermectin had signs of a weakened immune system, including reduced lymphocyte blastogenesis and reduced antibody response to human ovalbumin (Stankiewicz et al. 1995). However, rabbits exposed to ivermectin did not show any weakened immune system effects (Savanur et al. 1996). Halley et al. (1993) observed that ivermectin was slightly less toxic than abamectin when tested on laboratory animals. The oral LD_{50} values for ivermectin with the mouse and rats are about 2 and 50 mg/kg, respectively. However, oral LD_{50} values for abamectin are about 15 and 11 mg/kg for the mouse and the rat, respectively.

These chemicals have a great potential to affect wildlife through residues in the dung of treated animals. Avermectins could indirectly affect some species of vertebrates through reducing populations of the dung-inhabiting fauna as livestock dung is an important feeding habitat for a number of vertebrate species. Cow dung insects are an important dietary component of the chough (McCracken 1988). The dung insect *Aphodius* species account for 30% of the diet of greater horseshoe bat (Jones 1990). McCracken (1993) reported that the effects may be severe if they occur during the breeding or foraging of the young animals. Bloom and Matheson (1993) reported that ivermectins had little toxicity to birds. Halley et al. (1993) found that the abamectin LC_{50} values for bobwhite quail and mallard duck were 3102 ppm and 383 ppm, respectively. Alek-

sic et al. (1996) reported that ivermectin displayed no genotoxic effects on human lymphocytes. Clearly, avermectins may have some environmental effects on terrestrial organisms, but these are unlikely to be serious related to the residues reported in the literature.

I. Environmental Risk Assessment

It is not the aim of this review to present a formal environmental risk assessment (ERA) (for details, see Bloom and Matheson 1993; Römbke et al. 1996). However, to demonstrate the principles a short assessment is given here (Römbke et al. 2000). The general principle of an ERA is to compare predicted exposure (PEC) and effect (PNEC) values in an environmental compartment. If the former is higher than the latter (i.e., the PEC/PNEC ratio is >1), a risk for the environment cannot be ruled out. Among veterinary drugs, ivermectin is probably the compound with the most environmental data. An ERA was performed as early as 1986 (U.S. Federal Register, Vol. 51, no. 145). Since then, many studies (but a few according to standardized guidelines) have confirmed that exposure and effects of ivermectin are likely to happen in the environment. Labels are already in use to avoid damage to the aquatic compartment.

Exposure Analysis: Measured concentration in cow dung: 0.4–9 mg/kg
$\rightarrow$PEC = 9.0 mg/kg

Effect Analysis: LC_{50} from an acute tests (earthworm): 15.8–315 mg/kg
$\rightarrow$PNEC = 0.016 mg/kg

Risk-Characterization: PEC/PNEC – Ratio: 562 (EU Class 1)

When reassessing the environmental concentration of ivermectin (maximum, 1.70 mg/kg; Montforts, personal communication) and assuming that the low-effect concentration for earthworms (15.8 mg/kg) might not be valid, i.e. (Barth, personal communication), the PEC/PNEC ratio would still be greater than 1. Nevertheless, some refinement of the effect data seems to be necessary. For the fauna of the dung subcompartment a risk has been identified, whereas the soil compartment, in general, seems not to be affected. Significantly, the results of some field studies confirm a risk, but in other investigations no effects on the meadow ecosystem were reported. These seemingly contradictory results are probably caused by the application of different, usually not standardized, methods and by comparing different situations concerning the biocoenosis involved. It should be noted that the performance of an ERA for the compartment soil probably would have shown no risk. The inclusion of the subcompartment dung pad, however, revealed that there is a problem.

IV. Conclusions

It is very difficult to make a value judgment on the overall potential of avermectins to affect agroecosystems from the data currently available. The chemical persistence in dung and soil and the broad spectrum of activity against arthro-

pods indicate that if avermectins become used extensively, and reach the soil in appreciable quantities, they could cause two serious problems. The first effect is ecological, consisting of damage to the dung-inhabiting populations and consequent impact on other organisms, particularly because many dung insects are also active as pollinators (Skidmore 1991). In addition, when the larvae of dung insects become adult, as in *Scatophaga* species, the adults are predators of other insects. The second problem relates to cow pat decomposition, effects on dynamic soil processes, particularly the organic matter turnover, and the possibility of pasture fouling. The main environmental impact of the chemical seems to be that already studied, the effects on dung insects, dung decomposition, and the resulting increased potential for fouling of pastures and loss of productivity. More studies are needed to be able to assess the true extent of the problem and the severity of the impact.

In particular, further investigations of the effects of avermectins should be made using standardized test methods, probably by modifying existing tests (Herd 1995). These tests should focus particularly on chronic, sublethal parameters such as developmental and morphological or behavioral changes as well as sterility, as these are much more sensitive than the parameter of mortality used so far. In addition, the test modifications could be harmonized with those conditions already proposed for the performance of standardized decomposition tests. For example, Barth (1993) was correct when requiring that at least factors such as moisture, amount, and surface area should be standardized when testing dung. Other authors have demanded that such tests should be performed in different climatic and exposure situations (King 1993a). However, single-species tests are probably useful only if key species such as dung beetles or dipteran larvae are used (Moore and De Ruiter 1993). More appropriate would be a combined approach, studying the structure of the dung fauna community (focusing on the most important groups) as well as its function (especially dung decomposition) in parallel (perhaps in terrestrial microcosms).

Independently from further research, it should be asked whether exposure to avermectins could be decreased. In this context the use of those application methods that minimize environmental exposure must be mentioned [e.g., microdosage, ~1/1000 of the normal concentration of 0.2 mg/kg body w according to Pfister et al. (1994)]. An overview of the various possibilities concerning application and concentrations is given by Herd (1995). In a more general sense, the application of antiparasitic drugs could be minimized by using drugs with different action modes or by avoiding pasturing animals on meadows during the first several days after medication.

Summary

The avermectins are a group of insecticidal, acaricidal, and nematicidal pesticides used mainly for the control of horticultural pests and parasites and pests of domestic animals. They are high molecular weight, macrocyclic latories isolated from a fermentation broth of the soil actinorycete, *Streptomyces avertimi-*

lis. There are two main compounds, abamectin and ivermectin. They have a broad spectrum of activity, are hydrophobic, of low volatility and solubility, with a strong affinity to lipids, soil, and organic matter. They can persist in soils or organic media for several months or even possibly years, particularly under anaerobic conditions.

When abamectin is used against crop pests its effects include behavioral modifications, such as increased activity and feeding inhibition, reduced fecundity, and morphological aberations. Abamectin has been used against spider mites, leaf miners, fire ants, fruit flies, whiteflies, gypsy moth, diamondback moths, codling moths, and even nematodes. Because it is a broad-spectrum pesticide, there have been various reports of its toxic effects on natural enemies of pests.

Ivermectin is used against ecto- and endoparasites of domestic animals such as ticks, flies, sheep scab, nasal bots, sheep flies, tsetse flies, and gastrointestinal nematodes. Significant amounts of ivermectin and its residues are excreted in livestock feces. The pesticide binds tightly to organic matter in dung and retains biological activity for more than a year. There is abundant evidence that these residues are toxic to a range of dung-degrading insects, such as fly larvae, beetles and their larvae, stable flies, face flies, horn flies, and bush flies. There is considerable evidence that this toxicity may delay the rates of decomposition of dung, although the overall effects are complex and variable.

There is little evidence that avermectins have serious adverse effects on soil-inhabiting invertebrates such as earthworms. There is evidence, however, that avermectins that reach aquatic systems may affect fish and water-inhabiting invertebrates such as *Daphnia*. They may also affect sediment-inhabiting invertebrates. However, no serious overall effects on aquatic systems have been reported.

The only potentially serious environmental impacts of avermectins seem to be on dung degradation, although their chemical structures lipid affinity and persistence indicates a need for environmental vigilence.

References

Albrecht CP, Sherman M (1987) Lethal and sublethal effects of Avermectin B_1 on three fruit fly species (Diptera: Tephritidae). J Econ Entomol 80:344–347.

Aleksic N, Milutinovic M, Bakrac T (1996) Investigation of the genotoxic effects of ivermectin on human lymphocytes. Acta Vet (Belgr) 46:51–55.

Ali A, Xue R-D, Alam SK (1997) Ecotoxicological effects of abamectin (MK-936) on natural populations of selected invertebrates in man-made ponds. Med Entomol Zool 48:233–241.

Alvinerie M, Sutra JF, Galtier P, Lifschitz A, Virkel A, Sallovitz J, Lanusse C (1999) Persistence of ivermectin in plasma and faeces following administration of a sustained-release bolus to cattle. Res Vet Sci 66:57–61.

Anderson JR, Merritt RW, Loomis EC (1984) The insect-free cattle dropping and its relationship to increased dung fouling of rangeland pastures. J Econ Entomol 77: 133–141.

Apperson CS, Powell EE, Brawne M (1984) Efficacy of individual mound treatments of MK-936 and Andro against the red imported fire ant (Hymenoptera-Formicidae). J GA Entomol Soc 19:508–516.

Barth D (1993) Importance of methodology in the interpretation of factors affecting degradation of dung. Vet Parasitol 48:99–108.

Barth D, Schaper R (1992) Dungabbau. Der Abbau von Rinderdung nach Behandlung der Tiere mit Ivermectin. Vet 9/92.

Barth D, Heinze-Mutz EM, Roncalli RA, Schluter D, Gross SJ (1993) The degradation of dung produced by cattle treated with an ivermectin slow-release bolus. Vet Parasitol 48:215–227.

Barth D, Heinze-Mutz EM, Langholff W, Roncalli RA, Schlueter D (1994) Colonisation and degradation of dung pats after subcutaneous treatment of cattle with ivermectin or levamisole. Appl Parasitol 35:277–299.

Barth D, Rehbein S, Reid JFS, Barrick RA (1996) Efficacy of an in-feed formulation of ivermectin against adult worms and somatic larvae of *Strongyloides ransomi*. Vet Parasitol 65:89–97.

Beers EH, Anderson A, Brown RD (1996) Effect on leaf age on length of residual activity of abamectin in pome fruit foliage. J Econ Entomol 89:488–492.

Bloom RA, Matheson JC III (1993) Environmental assessment of avermectins by the US Food and Drug Administration. Vet Parasitol 48:281–294.

Bouwman GM, Reus JAWA (1994) Persistence of medicines in manure. CLM 163, 26 S. Centre for Agriculture & Environment,

Brownlee DJA, Holden-Dye L, Walker RJ (1997) Actions of the anthelmintic ivermectin on the pharyngeal muscle of the parasitic nematode, *Ascaris suum*. Parasitology 115: 553–561.

Burg RW, Stapley EO (1989) Isolation and characterization of the producing organism. In: Campbell WC (ed) Ivermectin and Abamectin. Springer-Verlag, New York.

Campbell WC (1985) Ivermectin: an update. Parasitol Today 1:10–16.

Campbell WC (1989) Ivermectin and Abamectin. Springer-Verlag, New York.

Campbell WC, Fisher MH, Stapley EO, Albers-Schonberg G, Jacob TA (1983) Ivermectin: a potent new antiparasitic agent. Science 221:823–828.

Campos F, Dybas RA, Krupa DA (1995) Susceptibility of two-spotted spider mite (Acari: Tetranychidae) populations in California to abamectin. J Econ Entomol 88:225–231.

Campos F, Krupa DA, Dybas RA (1996) Susceptibility of populations of two-spotted spider mites (Acari: Tetranychidae) from Florida, Holland, and the Canary Islands to abamectin and characterization of abamectin resistance. J Econ Entomol 89:594–601.

Clarke GM (1992) Fluctuating asymmetry: a technique for measuring developmental stress of genetic and environmental origin. Acta Zool Fenn 191:31–35.

Collier LM, Pinn EH (1998) An assessment of the acute impact of the sea lice treatment ivermectin on a benthic community. J Exp Mar Biol Ecol 230:131–147.

Cox DL, Knight AL, Biddinger DJ, Lasota JA, Pikounis B, Hull LA, Dybas RA (1995a) Toxicity and field efficacy of avermectins against codling moth (Lepidoptera: Tortricidae) on apples. J Econ Entomol 88:708–715.

Cox DL, Remick MD, Lasota JA, Dybas RA (1995b) Toxicity of avermectins to *Liriomyza trifolii* (Diptera: Agromyzidae) larvae and adults. J Econ Entomol 88:1415–1419.

Dadour IR, Cook DF, Neesam C (1999) Dispersal of dung containing ivermectin in

the field by *Onthophagus taurus* (Coleoptera: Scarabaeidae). Bull Entomol Res 89: 119–123.

Davies IM, McHenery JG, Rae GH (1997) Environmental risk from dissolved ivermectin to marine organisms. Aquaculture 158:263–275.

Davies IM, Gillibrand PA, McHenry JG, Rae GH (1998) Environmental risk of ivermectin to sediment-dwelling organisms. Aquaculture 163:29–46.

Davis JA, Paylor R, McDonald M, Libbey M, Ligler A, Bryant K, Crawley JN (1999) Behavioral effects of ivermectin in mice. Lab Anim Sci 49:288–296.

Deecher DC, Brenzer J, Tanenbaum SW (1987) Avermectin B_{1a} and Mibemycinas contact toxicants for gypsy moth (Lepidoptera: Lymantriidae) larvae and eggs. J Econ Entomol 80:1284–1287.

Di Pietro JA, Ewerrt KE, Todd KS (1993) Ivermectin treatment of horses: effect on the distribution of lawns and roughs in horse pastures. Vet Parasitol 48:241–246.

Distelmans W, D'Haeseleer F, Mortelmans J (1983) Efficacy of systemic administration of ivermectin against tsetse flies. Ann Soc Belge Med Trop 63:119–122.

Drummond RO (1985) Effectiveness of ivermectin for control of arthropod pests of livestock. Southwest Entomol Suppl 7:34–42.

Dybas RA (1989) Abamectin use in crop protection. In: Campbell WC (ed) Ivermectin and Abamectin. Springer-Verlag, New York.

El-Bagoury ME, El-Banhawy EM (1987) Effect of feeding treated prey with dicofol and avermectin on the survival, reproduction and development of the predacious mite *Phytoseius finitimus* (Acari, Phytoseiidae). J Appl Entomol 104:35–39.

Ewert KM, DiPietro JA, Danner CS Jr, Lawrence LM (1991) Ivermectin treatment of horses; effect on proportion of faecal-fouled areas in pastures. Vet Rec 129:140–141.

Fincher GT (1992) Injectable ivermectin for cattle: effects on some dung-inhabiting insects. Environ Entomol 21:871–876.

Fincher GT (1996) Ivermectin pour-on for cattle: effects on some dung-inhabiting insects. Southwest Entomol 21:445–450.

Floate KD (1998) Does a repellent effect contribute to reduced levels of insect activity in dung from cattle treated with ivermectin? Bull Entomol Res 88:291–297.

Floate KD, Fox AS (1999) Indirect effects of ivermectin residues across trophic levels: *Musca domestica* (Diptera: Muscidae) and *Muscidifurax zaraptor* (Hymenoptera: Pteromalidae). Bull Entomol Res 89:225–229.

Forbes AB (1993) A review of regional and temporal use of avermectins in cattle and horses worldwide. Vet Parasitol 48:19–28.

Forbes AB, Pitt SR, Baggott DG, Rehbein S, Barth D, Bridi AA, Carvalho LA, O'Brien DJ (1999) A review of the use of a controlled-release formulation of ivermectin in the treatment and prophylaxis of *Psoroptes ovis* infestations in sheep. Vet Parasitol 83:319–326.

Glancey BM, Lofgren GS, Williams DF (1982) Avermectin B_{1a}: effects on the ovaries of red imported fire ant queens (Hymenoptera: Formicidae). J Med Entomol 19:743–747.

Gopal RM, Pomroy WE, West DM (1999) Resistance of field isolates of *Trichostrongylus colubriformis* and *Ostertagia circumcincta* to ivermectin. Int J Parasitol 29:781–786.

Gover J, Strong L (1995) The effect of ivermectin in ingested cow-dung on the mortality and oviposition of the dung fly *Neomyia cornicing* (Diptera: Muscidae). Bull Entomol Res 85:53–57.

Gover J, Strong L (1996) Determination of the toxicity of faeces of cattle treated with

an ivermectin sustained-release bolus and preference trials using a dung fly, *Neomyia cornicia*. Entomol Exp Appl 81:133–139.

Grafius E, Hayden J (1988) Insecticide and growth regulator effects on the leafminer, *Liriomyza Trifolii* (Diptera: Agromyzidae), in celery and observations on parasitism. Great Lakes Entomol 21:49–54.

Grafton-Cardwell EE, Hoy MA (1983) Comparative toxicity of avermectin B_1 to the predator *Metaseiulus occidentalis* (Nesbitt) (Acari: Phytoseiidae) and the spider mites *Tetranychus urticae* Koch and *Panonychus ulmi* (Koch) (Acari: Tetranychidae). J Econ Entomol 76:1216–1220.

Guglielmone AA, Volpogni MM, Anziani OS, Flores SG (1999) Evaluation of injectable abamectin to control natural infestations of *Haematobia irritans* (Diptera: Muscidae) in cattle. J Med Entomol 36:325–328.

Gunn A, Sadd JW (1994) The effect of ivermectin on the survival, behaviour and cocoon production of the earthworm *Eisenia fetida*. Pedobiology 38:327–333.

Halley BA, Jacob TA, Lu AYH (1989a) The environmental impact of the use of ivermectin: environmental effects and fate. Chemosphere 18:1543–1563.

Halley BA, Nessel RJ, Lu AYH (1989b) Environmental aspects of ivermectin usage in livestock: general considerations. In: Campbell WC (ed) Ivermectin and Abamectin. Springer-Verlag, New York.

Halley BA, VandenHeuvel WJA, Wislocki PG (1993) Environmental effects of the usage of avermectins in livestock. Vet Parasitol 48:109–125.

Herd R (1995) Endectocidal drugs: ecological risks and counter-measures. Int J Parasitol 25:875–885.

Herd RP, Sams RA, Ashcraft SM (1996) Persistence of ivermectin in plasma and faeces following treatment of cows with ivermectin sustained-release, pour-on or injectable formulations. Int J Parasitol 26:1087–1093.

Holter P (1983) Effect of earthworms on the disappearance of cattle droppings. In: Satchell JE (ed) Earthworm Ecology.1st Ed. Chapman & Hall, London.

Holter P, Sommer C, Gronvold J, Madsen M (1993) Effects of ivermectin treatment on the attraction of dung beetles (Coleoptera: Scarabaeidae and Hydrophilidae) to cow pats. Bull Entomol Res 83:53–58.

Hoy MA, Cave FE (1985) Laboratory evaluation of avermectin as a selective acaricide for use with *Metaseilus occidentalis* (Nesbitt) (Acarina: Phytoseiidae). Exp Appl Acarol 1:139–152.

Hoy T, Horsberg TE, Nafstad I (1992) The disposition of ivermectin in Atlantic salmon (*Salmo salar*). In: Michel C, Alderman DJ (eds) Chemotherapy in Aquaculture: From Theory to Reality. Office Internationale des Epizooties, Paris, pp 461–467.

Ishaaya I, Yablonski S, Gurevitz E, Renneh S (1986) Toxicity of Avermectin B_1 to *Drosophila melanogaster* (Diptera: Drosophilidae) and *Lobesia botrana* (Lepidoptera: Tortricidae). J Econ Entomol 79:1621–1623.

Islam IM, Mostofa M, Rofiq K (1999) Efficacy of ivermectin (pour on formulation) against gastrointestinal nematodiasis in cattle of Bangladesh. Ind J Pharmacol 31: 234–236.

James PS, Picton J, Rilk RF (1980) Insecticidal action of the avermectins. Vet Rec 106: 59–.

Jansson RK, Rabatin S (1997) Curative and residual efficacy of injection applications of avermectins for control of plant-parasitic nematodes on banana. J Nematol 29: 695–702.

Johal M, Kaur M (1995) Chemophylactic studies with ivermectin on bovine nematode infection. Uttar Pradesh J Zool 15:67–69.

Jones G (1990) Prey selection by the greater horseshoe bat (*Rhinolophus ferrumequinum*): optimal foraging by echolcation? J Anim Ecol 59:587–602.

King KL (1993a) Methods for assessing the impact of avermectins on the decomposer community of sheep pastures. Vet Parasitol 48:87–97.

King KL (1993b) The potential for avermectins to affect the nutrient economy of grazed pastures. Vet Parasitol 48:261–271.

Krueger K, Scholtz CH (1995) The effect of ivermectin on the development and reproduction of the dung-breeding fly *Musca nevilli* Kleynhans (Diptera, Muscidae). Agric Ecosyst Environ 53:13–18.

Krueger K, Scholtz CH (1997) Lethal and sublethal effects of ivermectin on the dung-breeding beetles *Euoniticellus intermedium* (Reiche) and *Onitis alexis* Klug (Coleoptera, Scarabaeidae). Agric Ecosyst Environ 61:123–131.

Krueger K, Scholtz CH (1998) Changes in the structure of dung insect communities after ivermectin usage in a grassland ecosystem. I. Impact of ivermectin under drought conditions. Acta Oecol 19:425–438.

Larson RL, Corah LR, Spire MF, Cochran RC (1995) Effect of treatment with ivermectin on reproductive performance of yearling beef heifers. Theriogenology 44:189–197.

Lasota JA, Shelton AM, Bolognese JA, Dybas RA (1996) Toxicity of avermectins to diamondback moth (Lepidoptera: Plutellidae) populations: Implications for susceptibility monitoring. J Econ Entomol 89:33–38.

Lindley D (1987) Merck's new drug free to WHO for river blindness programme. Nature (Lond) 329:752.

Lucientes J, Castillo JA, Ferrer LM, Peribanez MA, Ferrer-Dufol M, Gracia-Salinas MJ (1998) Efficacy of orally administered ivermectin against larval stages of *Oestrus ovis* in sheep. Vet Parasitol 75:255–259.

Lumaret JP, Galante E, Lumbreras C, Mena J, Bertrand M, Bernal JL, Cooper JF, Kadiri N, Crowe D (1993) Field effects of ivermectin residues on dung beetles. J Appl Ecol 30:428–436.

Madsen M, Gronvold J, Nansen P (1988) Effects of treatment of cattle with some anthelmintics on the subsequent degradation of their dung. Acta Vet Scand 29:515–517.

Madsen M, Overgaard Nielsen B, Holter P, Brochner Jespersen OC, Vagn Jensen KM, Nansen P, Gronvold J (1990) Treating cattle with ivermectin: effects on the fauna and decomposition of dung pats. J Appl Ecol 29:349–356.

Mangels GD (1995) Environmental risk assessment for veterinary medicines by the FDA. In: Wolf PU (ed) Environmental Risk Assessment for Pharmaceuticals and Veterinary Medicines. RCC Group, Basel, pp 115–132.

Marley SE, Hall RD, Corwin RM (1993) Ivermectin cattle pour-on: duration of a single late spring treatment against honnflies, *Haematobia irritans* (L.) (Diptera: Muscidae) in Missouri, USA. Vet Parasitol 51:167–172.

McCracken DI (1988) Ivermectin in cow dung: possible adverse effects on the chough? In: Bignel E, Curtis DJ (eds) Choughs and Land-Use in Europe. Proceedings of an International Workshop on the Conservation of the Chough, *Pyrrhocorax pyrrhocorax*, in the EC.

McCracken DI (1993) The potential for avermectins to affect wildlife. Vet Parasitol 48: 273–280.

McCracken DI, Foster GN (1993) The effect of ivermectin on the invertebrate fauna associated with cow dung. Environ Toxicol Chem 12:73–84.

McKeand J (1988) Vet Rec 122:587–.
Meija M, Gonzalez-Iglesias A, Diaz-Torga GS, Villafane P, Formia N, Libertun C, Becu-Villalobos D, Lacau-Mengido IM (1999) Effects of continuous ivermectin treatment from birth to puberty on growth and reproduction in dairy heifers. J Anim Sci 77: 1329–1334.
Miller JA, Kunz SE, Oehler DD, Miller RW (1981) Larvicidal activity of Merck-933, and avermectin, against the horn fly, stable fly, face fly, and house fly. J Econ Entomol 74:608–611.
Miller JA, Garris GI, George JE, Oehler DD (1989) Control of lone star ticks (Acari: Ioxidae) on Spanish goats and white-tailed deer with orally administered ivermectin. J Econ Entomol 82:1650–1656.
Miller JE, Morrison DG (1992) Effect of fenbendazole and ivermectin on development of strongylate nematode eggs and larvae in calf feces. Vet Parasitol 43:265–270.
Moore JC, De Ruiter PC (1993) Assessment of disturbance on soil ecosystems. Vet Parasitol 48:75–85.
Morse JG, Bellows TS Jr, Gaston LK, Iwata Y (1987) Residual toxicity of acaricides to three beneficial species on California citrus. J Econ Entomol 80:953–960.
Munyua WK, Ng'ang'a CJ, Ngotho JW (1998) Efficacy of ivermectin delivered from a sustained-release bolus against gastrointestinal nematodes in field grazing calves in Nyandarua district of Kenya. Vet Parasitol 76:105–119.
O'Brien DJ, Forbes AB, Pitt SR, Baggott DG (1999) Treatment and prophylaxis of psoroptic mange (sheep scab) using an ivermectin intraruminal controlled-release bolus for sheep. Vet Parasitol 85:79–85.
Oksanen A, Norberg H, Nieminen M (1998) Ivermectin treatment did not increase slaughter weight of first-year reindeer calves. Prev Vet Med 35:209–217.
Park CG, Lee MH, Yoo JK, Lee JO, Choi BR (1995) Relative toxicity of abamectin to the predatory mite *Amblyseius womersleyi* Schicha (Acari: Phytoseiidae) and two-spotted spider mite *Tetranychus urticae* Koch (Acari: Tetranychidae). Korean J Appl Entomol 34:360–367.
Paulrud CO, Pederson RE, Eydal M (1997) Field efficacy of ivermectin (Ivomec) injection on faecal strongyle egg output of Icelandic horses. Buvisindi 11:131–139.
Pereira MD, Kohek I (1998) The efficacy of injectable ivermectin for the control of sarcoptic mange in pigs. Rev Bras Parasitol Vet 7:53–56.
Pfeifer C, Emmerling C, Schröder D, Niemeyer J (1998) Antibiotika (Ivermectin, Monensin) und endokrine Umweltchemikalien (Nonylphenol, Ethinylöstradiol) im Boden. UWSF—Z. Umweltchemie Ökotoxikol 10:147–153.
Pfister K, Charbon JL, Tarry DW, Pithan K (1994) Improvements in the control methods for warble-fly in cattle and goats. COST 811. European Commission, Brussels.
Pitt SR, Heinze-Mutz EM, Baggot DG, Barth D (1996) Control of established infections of parasitic nematodes in cattle by an ivermectin sustained-release intraruminal bolus. Helminthologia (Bratisl) 33:125–131.
Pulliam JD, Preston JM (1989) Safety of ivermectin on in target animals. In: Campbell WC (ed) Ivermectin and Abamectin. Springer-Verlag, New York.
Putter I, MacConnell JG, Preiser FA, Haidru AA, Ristich SS, Dybas RA (1981) Avermectins: novel insecticides, acaricides and nematicides from a soil microorganism. Experientia (Basel) 37:963–964.
Reed DK, Reed GL (1986) Activity of avermectin B_1 against the striped cucumber beetle (Coleoptera: Chrysomelidae). J Econ Entomol 79:943–947.
Rehbein S, Corba J, Pitt SR, Varady M, Langholff WK (1999) Evaluation of the anthel-

mintic efficacy of an ivermectin controlled-release capsule in lambs under field conditions in Europe. Small Ruminant Res 33:123–129.

Ridsdill-Smith TJ (1988) Survival and reproduction of *Musca vetustissima* Walker (Diptera: Muscidae) and a scarabeine dung beetle in dung of cattle treated with avermectin B_1. J Aust Entomol Soc 27:175–178.

Rohrer SP, Arena JP (1995) Ivermectin interactions with invertebrate ion channels. Molecular action of insecticides on ion channels. pp 264–283.

Römbke J, Knacker TH, Stahlschmidt-Allner P (1996) Studie über Umweltprobleme im Zusammenhang mit Arzneimitteln. UBA Berlin-Texte 60/96; 361 S.

Römbke J, Knacker TH, Teichmann H (2000) Ecotoxicological evaluation of pharmaceuticals. In: Daughton C, Jones-Lepp T (eds) Pharmaceuticals in the Environment. ACS-Books, San Francisco

Rugg D, Gogolewski RP, Barrick RA, Eagleson JS (1997) Efficacy of ivermectin controlled-release capsules for the control and prevention of nasal bot infestations in sheep. Aust Vet J 75:36–38.

Sams R (1993) Chemical assay of avermectins by high performance liquid chromatography with fluorescence detection. Vet Parasitol 48:59–66.

Savanur NHH, Krishnappa G, Sastry KNV, Narayana KK (1996) Effect of ivermectin on lymphocyte status in rabbits. Indian Vet J 73:501–503.

Schaper R, Liebisch A (1991) Einfluß eines systemisch wirkenden Antiparasitikums (Ivermectin) auf die Dungfauna und den Dengabbau der Rinder bei Weidehalftung. Tierärztl Umsch 46:12–18.

Schmidt CD (1983) Activity of an avermectin against selected insects in aging manure. Environ Entomol 12:455–457.

Shipp JL, Wang K, Ferguson G (2000) Residual toxicity of avermectin b_1 and pyridaben to eight commercially produced beneficial arthropod species used for control of greenhouse pests. Biol Control 17:125–131.

Sommer C, Nielsen O (1992) Larvae of the dung beetle *Onthophagus gazella* F. (Col., Scarabaeidae) exposed to lethal and sublethal ivermectin concentrations. J Appl Entomol 114:502–509.

Sommer C, Steffansen B (1993) Changes with time after treatment in the concentrations of ivermectin in fresh cow dung and in cow pats aged in the field. Vet Parasitol 48: 67–73.

Sommer C, Steffansen B, Overgaard Nielsen B, Gronvold J, Vagn Jensen KM, Brochner Jespersen J, Springborg J, Nansen P (1992) Ivermectin excreted in cattle dung after subcutaneous injection or pour-on treatment: concentrations and impact on dung fauna. Bull Entomol Res 82:257–264.

Sommer C, Gronvold J, Holter P, Madsen M, Nansen P (1993a) Dung burial activity and development of ivermectin exposed *Diastellopalpus quinquedens* in a field experiment. Entomol Exp Appl 66:83–89.

Sommer C, Gronvold J, Holter P, Nansen P (1993b) Effects of ivermectin on two afrotropical dung beetles, *Onthophagus gazella* and *Diastellopalpus quinquedens* (Coleoptera: Scarabaeidae). Vet Parasitol 48:171–179. Entomol Exp Appl 66:83–89.

Spaepen KRI, Van Leemput LJJ, Wislocki PG, Verschueren C (1995) A uniform procedure to estimate the predicted environmental concentration (PEC) of the residues of veterinary medicines in soil. Environ Toxicol Chem 16:1977–1982.

Stankiewicz M, Cabaj W, Jonas WE, Moore LG, Millar K, Ng Chie W (1995) Influence of ivermectin on cellular humoral immune responses of lambs. Vet Immunol Immunopathol 44:347–358.

Steel JW (1993) Pharmacokinetics and metabolism of avermectins in livestock. Vet Parasitol 48:45–57.
Strong L (1986) Inhibition of pupariation and adult development in *Calliphora vomitoria* treated with ivermectin. Entomol Exp Appl 41:157–164.
Strong L (1989) Sequential latent effects of a sub-lethal dose of ivermectin in *Calliphora vomitoria* L. Pestic Sci 27:253–260.
Strong L (1992) Avermectins: a review of their impact on insects of cattle dung. Bull Entomol Res 82:265–274.
Strong L (1993) Overview: the impact of avermectins on pastureland ecology. Vet Parasitol 48:3–17.
Strong L, Brown TA (1987) Avermectins in insect control and biology: a review. Bull Entomol Res 77:357–389.
Strong L, Wall R (1988) Ivermectin in cattle treatment: non-specific effects on pastureland ecology. Asp Appl Biol 17:231–238.
Strong L, Wall R (1994) Effects of ivermectin and moxidectin on the insects of cattle dung. Bull Entomol Res 84:403–409.
Strong L, Wall R, Woolford A, Djeddour D (1996) The effect of faecally excreted iveremctin and fenbendazole on the insect colonisation of cattle dung following the oral administration of sustained-release boluses. Vet Parasitol 62:253–266.
Thain JE, Davies IM, Rae GH, Allen YT (1997) Acute toxicity of ivermectin to the lugworm *Arenicola marina*. Aquaculture 159:47–52.
Tzeng CC, Kao SS (1999) Toxicity of nine insecticides to *Eretmocerus orientalis* adults—a parasitoid of silverleaf whitefly *(Bemisia argentifolii)*. Plant Prot Bull (Taichung) 41:83–86.
Uzuka Y, Yoshioka T, Tanabe S, Kinoshita G, Nagata T, Yagi K, Funaki H, Hanyo H, Sarashina T (1999) Chemical control of *Haematobia irritans* with 0.5% topical ivermectin solution in cattle. J Vet Med Sci 61:287–289.
Van Den Heuvel WJA, Forbis AD, Halley BA, Ku CC (1996) Bioconcentration and depuration of avermectin B_{1a} in the bluegill sunfish. Environ Toxicol Chem 15:2263–2266.
Wall R, Strong L (1987) Environmental consequences of treating cattle with the antiparasitic drug ivermectin. Nature (Lond) 327:418–421.
Wall R, Strong L (1988) Ivermectin and cattle dung—a case for concern. Parasitol Today 4:107–108.
Walsh DB, Zalom FG, Shaw DV, Welch NC (1996) Effect of strawberry plant physiological status on the translaminar activity of avermectin B-1 and its efficacy against two-spotted spider mite (Acari: Tetranychidae). J Econ Entomol 89:1250–1253.
Wardhaugh KG, Mahon RJ (1991) Avermectin residues in sheep and cattle dung and their effects on dung-beetle (Coleoptera: Scarabaeidae) colonization and dung burial. Bull Entomol Res 81:333–339.
Wardhaugh KG, Mahon RJ (1998) Comparative effects of abamectin and two formulations of ivermectin on the survival of larvae of a dung-breeding fly. Aust Vet J 76: 270–272.
Wardhaugh KG, Holter P, Whitby WA, Shelley K (1996) Effects of drug residues in the faeces of cattle treated with injectable formulations of ivermectin and moxidectin on larvae of the bush fly, *Musca vetustissima* and the house fly, *Musca domestica*. Aust Vet J 74:370–374.
Whittier JC, Weech BL, Lucy MC, Keisler DH, Smith MF, Corwin RM (1999) Effect

of anthelmintic treatment on sexual maturation in prepubertal beef heifers. J Anim Sci 77:736–741.

Williams JC (1997) Anthelmintic treatment strategies: current status and future. Vet Parasitol 72:461–470.

Wislocki PG, Grosso LS, Dybas RA (1989) Environmental aspects of abamectin use in crop protection. In: Campbell WC (ed) Ivermectin and Abamectin. Springer-Verlag, New York.

Wratten SD, Mead-Briggs M, Gettinby G, Ericsson G, Baggott DG (1993) An evaluation of the potential effects of ivermectin on the decomposition of cattle dung pats. Vet Rec 133:365–371.

Wright DJ, Iqbal M, Verkerk RHJ (1995) Resistence to *Bacillus thuringiensis* and abamectin in the diamondback moth, *Plutella xylostella:* a major problem for integrated pest management? Meded Fac Landbouwkd Toegep Biol Wet Univ Gent 60:927–933.

Manuscript received November 3; accepted November 10, 2000.